Study and applications of induced Pluripotent Stem cells (iPS cells)

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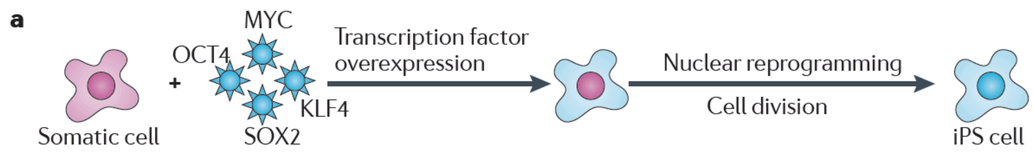
Embryonic stem cells (ES cells) have two principal characteristics: they can divide themselves indefinitely and have the ability to differentiate in any cell type. Obtaining these cells trigger an ethical debate because the destruction of a human embryo is needed. That's the reason why new technologies have obtain pluripotent cells by reprograming somatic cells: these cells are named induced pluripotent stem cells (iPS cells).

Objectives

- Identify what iPS cells are and how we can obtain them
- Describe the role of inducing reprograming factors (OSKM)
- Compare characteristics between embryonic stem cells, tumour cells and iPS cells
- Mention applications and medical uses of iPS cells

What are iPS cells?

iPS cells are somatic cells, which have been **reprogramed** by the overexpression of defined factors: **OSKM**

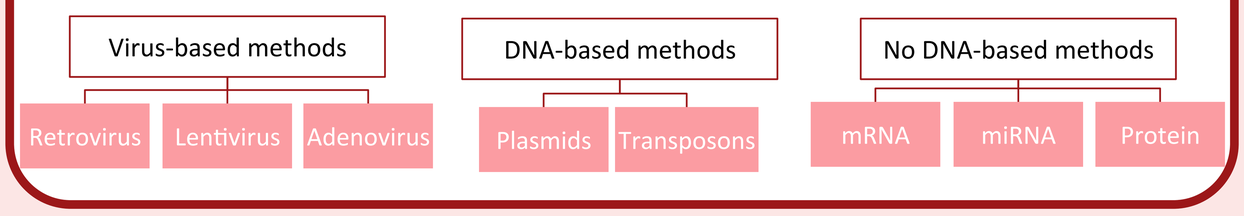


*OSKM: Oct 3/4, Sox2, Klf-4 i c-Myc

Fig.1 Experimental approach to nuclear reprogramming. (Jullien et at, 2011)

Methods to obtain iPS cells

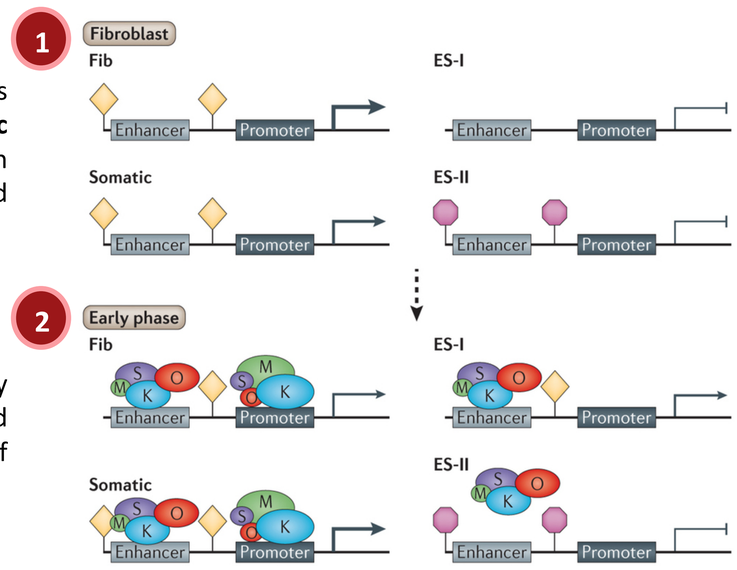
OSKM factors can be introduced into cells by different methods:



OSKM cocktail

OSKM factors bind different promoters and enhancers causing **epigenetic changes** in histones. Genes involved in cell phenotype are silenced and pluripotency genes become active.

Unfortunately, reprograming efficiency is low; a **maturation process** is required to acquire a total expression of pluripotency marks.



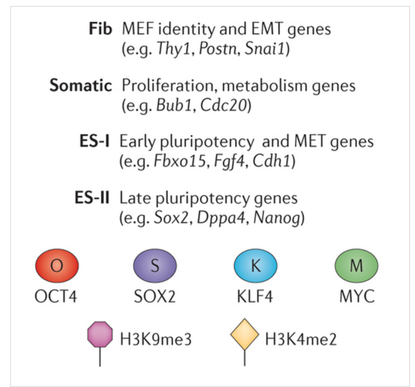


Fig. 2 Epigenome remodelling by OSKM factors (Burganim et al. 2013)

iPS cells compared with ES cells and tumour cells

The main objective of generating iPS cells is obtaining cells as similar as possible with ES cells. Although many characteristics are alike between these two types of pluripotent cells, iPS cells show some **Epigenetic memory** that can disturb in further applications. In addition, iPS cells also share some traits with tumour cells, which contribute to complications in medical uses.

Competences shared with ES cells	Competences shared with tumour cells
▪ Chromatin structure ▪ Methylation pattern ▪ Gene expression ▪ Pluripotency	▪ High proliferation ▪ Genomic instability (causing mutations and chromosome aberrations)

Applications and medical uses

There exist multiple and advantageous applications of iPS cells, both in basic research and medical uses.

- **Cells from any tissue** in the body, even from difficult access organs, such as neurons or cardiomyocytes can be obtained.
- They allow to **reduce** the generation of **animal models**
- Studies of human pathologies become **more reliable**
- **New drug tests** with patient-derived cells can be performed in preclinical trials
- Waiting periods and donors for **organ and tissue transplants** can be reduced
- They do not show **immunological rejection**

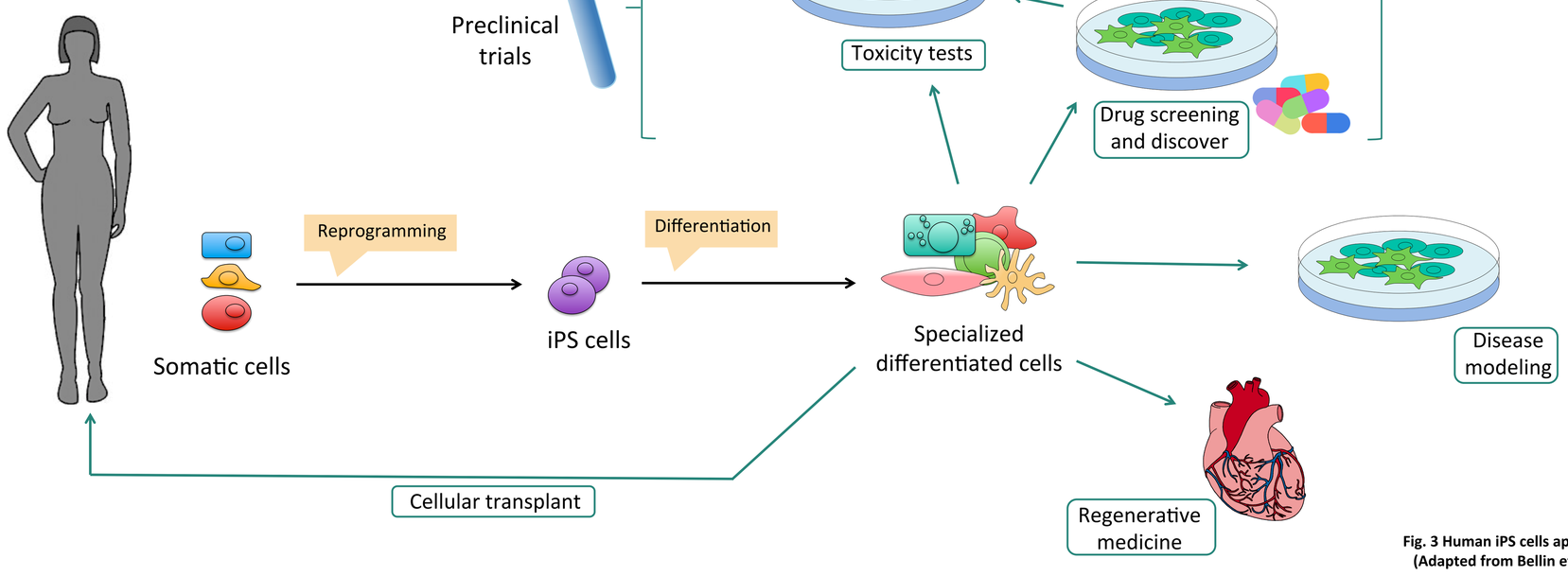


Fig. 3 Human iPS cells applications (Adapted from Bellin et al. 2012)

Conclusions

- iPS cells, which come from reprograming processes of somatic cells, are a viable alternative to embryonic stem cells, without ethical implications.
- These new cells open the door to new perspectives into biomedicine and regenerative medicine, but also to basic research and molecular studies of diseases.
- Current research in this field is very active. There are still many things to solve, especially to prevent the tumour potential of iPS cells.

Relevant references

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